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09/420,046

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10/18/99

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John SemiKlose  
Signature

John SemiKlose  
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703-979-1111

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09/420,046

OCT 18, 1999

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United States Patent Application Publication No. \_\_\_\_\_, page, \_\_\_\_\_ line \_\_\_\_\_,

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US006558708B1

(12) **United States Patent**  
**Lin**(10) **Patent No.:** **US 6,558,708 B1**  
(45) **Date of Patent:** **May 6, 2003**(54) **METHODS FOR MANIPULATING UPPER GASTROINTESTINAL TRANSIT, BLOOD FLOW, AND SATIETY, AND FOR TREATING VISCERAL HYPERALGESIA**WO 94/03380 3/1994  
WO 96/18374 11/1996  
WO 98/56397 A1 12/1998  
WO 85/02840 A1 7/1999(75) **Inventor:** **Henry C. Lin, Manhattan Beach, CA (US)**(73) **Assignee:** **Cedars-Sinai Medical Center, Los Angeles, CA (US)**(\*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.(21) **Appl. No.:** **09/546,119**(22) **Filed:** **Apr. 10, 2000****Related U.S. Application Data**

(63) Continuation-in-part of application No. 09/420,046, filed on Oct. 18, 1999, which is a continuation-in-part of application No. 09/359,583, filed on Jul. 22, 1999, now abandoned, which is a continuation of application No. 08/832,307, filed on Apr. 3, 1997, now Pat. No. 5,977,175, which is a continuation of application No. 08/442,843, filed on May 17, 1995, now abandoned.

(51) **Int. Cl.<sup>7</sup>** ..... **A61K 9/16; A61K 9/20; A61K 9/14; A61K 9/48**  
(52) **U.S. Cl.** ..... **424/490; 424/451; 424/464; 424/474; 424/489**  
(58) **Field of Search** ..... **424/451, 463, 424/464, 474, 489, 490, 491; 514/12, 13**(56) **References Cited****U.S. PATENT DOCUMENTS**4,160,452 A 7/1979 Theeuwes  
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Dobson et al., The Effect of Oleic Acid on the Human Ileal Break and Its Implications for Small Intestinal Transit of Table Formulations, *Pharmacol. Research*, vol. 16, pp 92-96 (1999), No. 1.\*

(List continued on next page.)

**Primary Examiner**—Thurman K. Page**Assistant Examiner**—S. Tran(74) **Attorney, Agent, or Firm**—Sidley Austin Brown & Wood LLP

(57)

**ABSTRACT**

Disclosed are a method of manipulating the rate of upper gastrointestinal transit of a substance in a mammal. Also disclosed are methods of manipulating satiety and post-prandial visceral blood flow. A method of treating visceral pain or visceral hypersensitivity in a human subject is also described. A method for prolonging the residence time of an orally or enterally administered substance by promoting its dissolution, bioavailability and/or absorption in the small intestine is also described. These methods are related to a method of transmitting to and replicating at a second location in the central nervous system a serotonergic neural signal originating at a first location in the proximal or distal gut of a mammal and/or a method of transmitting to and replicating at a second location in the upper gastrointestinal tract a serotonergic neural signal originating at a first location in the proximal or distal gut.

**13 Claims, 6 Drawing Sheets**